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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,981	01/23/2001	Ejvind Jensen	4343.214-US	2751

7590 04/21/2003

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EXAMINER
ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/21/2003

20

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKET (check off ✓) ☐

ATTY:

TNAB DCKT 5/5/03

Office Action Summary	Application No.	Applicant(s)	
	09/767,981	JENSEN ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *15-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed January 21, 2003 (Paper No. 9) has been entered.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 14-22 have been renumbered 15-23.

Claims 15-23 are pending. Applicant elected with traverse the species phenol, and the species zinc in Paper No. 6. Claims 15-23 are being examined to the extent that they read upon the species phenol and the species zinc.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 15-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for GLP-1, does not reasonably provide enablement for GLP-1 compounds. Applicant argues that the specification discloses GLP-1 compounds and how to use such compounds; it is well settled that a patent need not disclose and preferably omits that which is well known in the art. Applicant's arguments have been fully considered but they are not persuasive. Applicant's arguments, focus almost exclusively on the level of ordinary skill in the art, and ignore the essence of the enablement requirement. Patent protection is granted in return for an enabling disclosure of the invention, not for vague intimations of general ideas that may

not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in this specification with respect to a GLP-1 compound. It is true, as Applicant argues, that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Claims 15-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant argues that the specification reasonably conveys what distinguishing attributes are shared by members of the genus. Applicant's arguments have been fully considered but they are not persuasive. The term GLP-1 compound also comprises

analogs and functional derivatives of GLP-1 (sentence bridging pages 1-2). Neither "analogs and functional derivatives of GLP-1" nor "GLP-1 compound" describes the common attributes or characteristics that identify members of the genus.

Claims 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, over the recitation of the term "GLP-1 compound". Applicant argues that the term "GLP-1 compound" has a clear and definite meaning. Applicant's arguments have been fully considered but they are not persuasive. The term GLP-1 compound also comprises analogs and functional derivatives of GLP-1 (sentence bridging pages 1-2). Neither "analogs and functional derivatives of GLP-1" nor "GLP-1 compound" identifies that material element or combination of elements which is unique to, and, therefore, definitive of a GLP-1 compound.

Applicant's traversal of the prior art rejections has been considered but it is moot in view of the new grounds of rejection below.

New formal matters, objections, and/or rejections:

Claim Rejections - 35 USC § 103

Claims 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Danley (4, cited by Applicants) in view of Avis (u10), and further in view of Galloway (a13), Schott (y7), and Ballard (x7).

Danley teaches a low solubility form of GLP-1(7-37) prepared by combining GLP-1(7-37) at from 2-15 mg/ml in buffer at pH 7-8.5 with a solution of a metal ion salt to obtain

solutions with from 1-8 mg/ml GLP-1(7-37) at molar ratios of about 1:1 to 270:1 zinc to GLP-1(7-37) (page 35, Example 34). 8 mg/ml GLP-1(7-37) is not less than about 10 mg/ml or not more than about 100 mg/ml of a GLP-1 compound. The low solubility form of GLP-1(7-37) does not contain less than a molar ratio of 0.4:1 zinc to GLP-1(7-37), between 0.4 and 0.1:1 zinc to GLP-1(7-37), or between 0.1 and 0.2:1 zinc to GLP-1(7-37). However, Danley teaches that prolonged delivery formulations of GLP-1 can be formulated with compositions comprising GLP-1(7-37) (page 12, line 57, through page 14, line 4), a phenolic compound, and zinc (page 14, lines 6-9) wherein the phenolic compound is phenol (page 19, line 5), wherein the molar ratio of zinc to GLP-1(7-37) is 0.1 to 6 (page 19, lines 5-6). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a low solubility form of GLP-1(7-37) prepared by combining GLP-1(7-37) at from 2-15 mg/ml in buffer at pH 7-8.5 with a solution of a metal ion salt to obtain solutions with from 1-8 mg/ml GLP-1(7-37) at molar ratios of about 1:1 to 270:1 zinc to GLP-1(7-37), and to modify that teaching by using a molar ratio of zinc to GLP-1(7-37) of 0.1 to 6 with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because a molar ratio of zinc to GLP-1(7-37) of 0.1 to 6 is useful for the preparation of prolonged delivery formulations of GLP-1(7-37).

Danley does not teach a low solubility form of GLP-1(7-37) prepared by combining GLP-1(7-37) at from 2-15 mg/ml in buffer at pH 7-8.5 with a solution of a metal ion salt and a phenolic compound to obtain solutions with from 1-8 mg/ml GLP-1(7-37) at molar ratios of 0.1 to 6 zinc to GLP-1(7-37) and a phenolic compound. However, Danley does teach that a prolonged delivery formulation being an aqueous suspension of insulinotropin precipitates or

aggregates can be formed by using precipitants for example, phenolic compounds or basic polypeptides or metal ions or salts, and/or by using high shear and that more than one precipitant can be used at one time (page 18, lines 43-45).

Avis teaches antimicrobial agents must be added to multi-dose parenteral preparations and phenol is a suitable antimicrobial agents (page 1550, column 1). Avis does not teach a low solubility form of GLP-1(7-37) prepared by combining GLP-1(7-37) at from 2-15 mg/ml in buffer at pH 7-8.5 with a solution of a metal ion salt and a phenolic compound to obtain solutions with from 1-8 mg/ml GLP-1(7-37) at molar ratios of 0.1 to 6 zinc to GLP-1(7-37) and a phenolic compound. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a low solubility form of GLP-1(7-37) prepared by combining GLP-1(7-37) at from 2-15 mg/ml in buffer at pH 7-8.5 with a solution of a metal ion salt to obtain solutions with from 1-8 mg/ml GLP-1(7-37) at molar ratios of 0.1 to 6 zinc to GLP-1(7-37), as taught by Daley, and to modify that teaching by adding a phenolic compound, as taught by Avis, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to prevent the multiplication of microorganisms inadvertently introduced into the formulation.

Danley in view of Avis are silent regarding the thixotropic properties of the formulation.

Galloway teaches that only a small quantity of zinc is required to complex with and precipitate a significant portion of the GLP-1 molecules (column 12, lines 23-25).

Schott teaches that thixotropy is particularly useful in the formulation of pharmaceutical suspensions and emulsions; thixotropy can be used to solve the dilemma involving low viscosity and rapid settling of solid particles in suspensions and rapid creaming of emulsions; thixotropy

prevents sedimentation and claying of suspended particles; Schott also teaches thixotropic agents (page 318, column 1, full paragraph 1)..

Ballard gives a clear indication of success in designing a sustained- or prolonged-action preparation with thixotropic "pellets" and teaches the advantages thereof. See Ballard page 1610, column 1, first paragraph, and column 2, full paragraphs 1-3.

Galloway, Schott, and Ballard do not teach a thixotropic composition comprising GLP-1. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a composition comprising GLP-1, a phenolic compound, and zinc, as taught by Danley in view of Avis, and to modify that teaching by making a thixotropic composition, as taught by Schott and/or Ballard, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because only a small quantity of zinc is required to complex with and precipitate a significant portion of GLP-1 and a thixotropic composition would prevent sedimentation and claying of the precipitated GLP-1 particles. When the suspension is shaken prior to use it becomes fluid enough to pass through a hypodermic needle.

The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

Prior to the present amendment none of the claims required the presence of a phenolic compound and thixotropy or a phenolic compound, zinc, and thixotropy. Amendment of the claims to require the presence of a phenolic compound and thixotropy or a phenolic compound,

zinc, and thixotropy necessitated the new ground(s) of rejection. Accordingly, Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
APRIL 19, 2003

The United States Patent and Trademark Office has changed certain mailing addresses!

Effective May 1, 2003

Use the address **provided in this flyer after May 1, 2003** for **any correspondence** with the United States Patent and Trademark Office (USPTO) in patent-related matters **to organizations reporting to the Commissioner for Patents.**

DO NOT USE the Washington DC 20231 and P.O. Box 2327 Arlington, VA 22202 addresses after May 1, 2003 for **any correspondence** with the USPTO even if these old addresses are indicated in the accompanying Office action or Notice or in any other action, notice, material, form, instruction or *other* information.

Correspondence in patent-related matters **to organizations reporting to the Commissioner for Patents** must now be addressed to:

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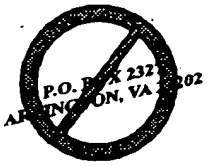

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Also effective May 1, 2003, the **USPTO is changing the special Box designations for Patents and Trademarks to corresponding Mail Stop designations** (*e.g.*, "Box 4" will now be "Mail Stop 4").

For further information, see *Correspondence with the United States Patent and Trademark Office*, 68 *Fed. Reg. 14332* (March 25, 2003). A copy of the *Federal Register* notice is available on the USPTO's web site at http://www.uspto.gov/web/menu/current.html#register

A listing of specific USPTO mailing addresses (See Patents – specific) will be available on the USPTO's web site on April 15, 2003 at http://www.uspto.gov/main/contacts.htm

Persons filing correspondence with the Office should check the rules of practice, the Official Gazette, or the Office's Internet Web site (www.uspto.gov) to determine the appropriate address and Mail Stop Designation (if applicable) for all correspondence being delivered to the USPTO via the United States Postal Service (USPS).

Questions regarding the content of this flyer should be directed to the Inventor Assistance Center at (703) 308-4357 or toll-free at 1-800-786-9199.

Revised Notice*
AMENDMENTS MAY NOW BE SUBMITTED IN REVISED FORMAT

The United States Patent and Trademark Office (USPTO) is permitting applicants to submit amendments in a revised format as set forth below. Further details of this practice are described in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, signed January 31, 2003, expected to be published in *Official Gazette* on February 25, 2003 (Notice posted on the Office's web site at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The revised amendment format is essentially the same as the amendment format that the Office is considering adopting via a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. The Office plans to adopt such a revision to 37 CFR 1.121 by July of 2003, at which point compliance with revised 37 CFR 1.121 will be mandatory.

Effective immediately, **all** applicants may submit amendments in reply to Office actions using the following format. Participants in the Office's electronic file wrapper prototype[1] receiving earlier notices of the revised practice may also employ the procedures set out below.

REVISED FORMAT OF AMENDMENTS

Begin on separate sheets:
Each section of an Amendment (e.g., Claim Amendments, Specification Amendments, Drawing Amendments, and Remarks) should begin on a separate sheet. *For example*, in an amendment containing a.) introductory comments, b.) amendments to the claims, c.) amendments to the specification, and d.) remarks, each of these sections must begin on a separate sheet. This will facilitate the process of separately indexing and scanning of each part of an amendment document for placement in an electronic file wrapper.

Two versions of amended part(s) no longer required:
The current requirement in 37 CFR 1.121(b) and (c) to provide two versions (a clean version and a marked up version) of each replacement paragraph, section or claim will be waived where an amendment is submitted in revised format below. The requirements for substitute specifications under 37 CFR 1.125 will be retained.

A) **Amendments to the claims:**
Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number by one of the following: (original), (currently amended), (previously amended), (canceled), (withdrawn), (new), (previously added), (reinstated – formerly claim #_), (previously reinstated), (re-presented – formerly dependent claim #_), or (previously re-presented). The text of all pending claims under examination must be submitted each time any claim is amended. Canceled and withdrawn claims should be indicated by only the claim number and status.
(2) All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim should be shown by strikethrough (for deleted matter) or underlining (for added matter). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended" will include markings.
(3) The text of pending claims not being amended must be presented in clean version, i.e., without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version.

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[1] The Office's Electronic File Wrapper prototype program is described in *USPTO ANNOUNCES PROTOTYPE OF IMAGE PROCESSING*, 1265 *Off. Gaz. Pat. Office* 87 (Dec. 17, 2002) ("Prototype Announcement"), and applies only to Art Units 1634, 2827 and 2834.

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FEB 20 2003

Dear Patent Business Customer:

The United States Patent and Trademark Office ("Office") is now permitting and encouraging applicants to voluntarily submit amendments in a revised format as set forth in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, ____ *Off. Gaz. Pat. Office* __ (February 25, 2003), currently available on the USPTO web site at **http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm**. The revised format permits amendments to the specification and claims to be made in a single marked-up version; the requirement for a clean version is eliminated. Attached, you will find a flyer with information and instructions regarding the procedures to be used to comply with the revised format. The flyers are being inserted with out-going Office actions mailed during the period of February 20, 2003 - March 31, 2003.

The revised amendment format is essentially the same as the amendment format for the specification, claims, and drawings that the Office is considering adopting via a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. This proposed revision and others necessary to facilitate a gradual transition to the use of an Electronic File Wrapper (EFW) will be set forth in a Notice of Proposed Rule making (NPR), expected to be published by March 2003. After consideration of public comments, the Office anticipates adopting a revision to § 1.121, following publication of a Notice of Final Rule making (NFR), expected by June 2003, at which point compliance with revised § 1.121 will be mandatory.

The Office will continue to accept your amendment submissions in the revised format during the voluntary period, which will extend up to the effective date of final revisions to § 1.121. The Office also encourages your feedback on the proposed revised amendment format and other changes set forth in the NPR, expected to be published by March 2003.

For assistance: Any questions regarding the submission of amendments pursuant to the revised practice should be directed to Office of Patent Legal Administration (OPLA), Legal Advisors Elizabeth Dougherty (**Elizabeth.Dougherty@uspto.gov**), Gena Jones (**Eugenia.Jones@uspto.gov**) or Joe Narcavage (**Joseph.Narcavage@uspto.gov**). Alternately, you may send e-mail to "Patent Practice", the OPLA e-mail address that has been established for receiving queries and questions about patent practice and procedures or telephone OPLA at (703) 305-1616.

Nicholas P. Godici
Commissioner for Patents

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